Chemistry & Biology

In This Issue

Synthetic Genetics Opens New Worlds

PAGE 1360

Synthetic genetics aims to explore the structural and functional properties of synthetic genetic polymers by in vitro evolution. Chaput et al. review recent advances in the Darwinian evolution of artificial genetic polymers and their potential applications in exobiology, molecular medicine, and synthetic biology.

Raman Imaging of Lipid Droplets

PAGE 1373

Lipid droplets are important players in cellular metabolism and related to growing menaces: obesity and diabetes. Noothalapati Venkata and Shigeto demonstrate simultaneous chemical visualization of lipid droplets and proteome in a single living yeast cell by combining time-lapse Raman imaging and ^{13}C-labeling.

Tailoring Jadomycin

PAGE 1381

Jadomycin B is a member of an atypical angucycline antibiotic family whose biosynthesis involves a unique ring opening C-C bond cleavage reaction. Fan et al. identified JadG as the enzyme catalyzing this ring opening reaction, the first verified member of a new enzyme class catalyzing an unprecedented C-C bond cleavage reaction.

Redox Sensing in AD

PAGE 1391

Methylene blue (MB) reduces accumulation of tau, which makes it a viable drug for Alzheimer's disease (AD), although the mechanism behind this is unclear. Miyata et al. report that MB acts through oxidation of the stress-inducible chaperone Hsp72 and suggest that MB's anti-AD activity involves Hsp72 redox sensing.

Proteins Only, Please

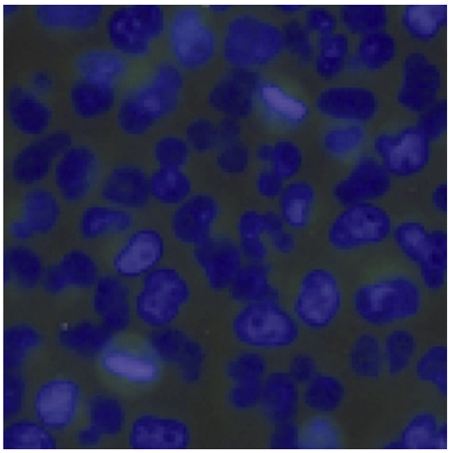
PAGE 1400

DeSantis and Shorter demonstrate how Hsp104, a protein disaggregase, drives prion strain selection events that favor Sup35 prions that encode strong (*PSI+*). Thus, proteostasis network can directly drive prion strain selection, which has implications for eliminating deleterious prions and self-templating amyloids.

How Cyanobactins Mature

PAGE 1411

Two proteases, PatA and PatG, work sequentially to generate a macrocyclizing backbone amide bond of circular peptides patellamides. Agarwal et al. determine their structures, identify new features that confer the activity upon PatG, and engineer PatG to yield a biocatalyst for the synthesis of circular peptides.



TGFβ/BMP Signaling Controlled by R-Smad Deubiquitination

PAGE 1423

Regulatory Smads (R-Smads) are central mediators of TGFβ and BMP signaling. Cheng et al. find that indirubin derivative E738 inhibits TGFβ and BMP pathways through ubiquitin-mediated depletion of total R-Smads. They reveal a novel mechanism for controlling TGFβ/BMP signaling via R-Smad protein deubiquitination.

Macropinocytosis Gets a Stimulus

PAGE 1437

Tanaka et al. found that CXCR4 serves as a receptor that stimulates internalization of the cell-penetrating peptide (CPP), an arginine 12-mer. Additionally, stimulating CXCR4 with its intrinsic ligands induced macropinocytosis. Both insights have relevance for better understanding of cellular uptake of CPPs.

Secondary Metabolites Fuels the Myxococci

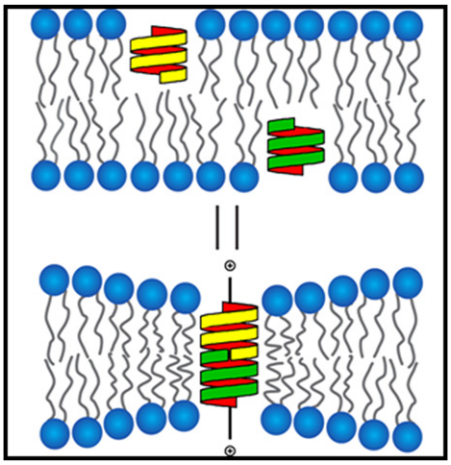
PAGE 1447

Volz et al. introduce two bacterial enhancer binding proteins (bEBP) as transcriptional regulators of secondary metabolites in *M. xanthus*. The approach increases yield of metabolites and shows the link between development, motility, predation, and secondary metabolite production at the transcriptional level.

To Antiport or To Channel, It is a Question Now

PAGE 1460

Howery et al. describe the first small-molecule inhibitor of CLC antiporters, OADS, and characterize the mechanism of inhibition. Inhibition requires OADS binding at two discrete sites, away from the Cl^--permeation pathway, suggesting that OADS might affect the H^+ pathway, the membrane, and/or CLC conformation.



Recycling Cell Wall through Active Site Plasticity

PAGE 1471

NagZ is a glycosidase that participates in recycling cell wall peptidoglycan during bacterial growth and activates β-lactam resistance in many bacteria. Bacik et al. describe structural snapshots along the reaction coordinate of NagZ, revealing unprecedented structural plasticity within the active site.

Mapping Out the Antibiotics Space

PAGE 1483

Wong et al. establish a new antibiotic profiling strategy, BioMAP (antibiotic mode of action profiling), using a panel of clinically relevant bacterial strains to create unique biological fingerprints for all major classes of antibiotics and discover new naphthoquinone-based compound with antibiotic activity.

